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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK
600 SOUTH AVENUE WEST
WESTFIELD, NJ 07090

EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,861	ASHLEY ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/2006 and 12/11/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on 5/04/2009 is acknowledged. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 15-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/04/2009.

3. Applicant's election with traverse of budesonide in the reply filed on 5/04/2009 is also acknowledged. Upon further consideration, the requirement for election as to this species is withdrawn. Accordingly, both budesonide and beclomethasone dipropionate as glucocoriticosteroids to be sterilized by the method will be considered and which reads on claims 1-14. Applicant timely traversed the election requirement in the reply filed on 5/04/2009.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. **Claims 1-7 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by *McAffer et al* (US 2003/0103864).**

6. Instant claim 1 is drawn to a method for the sterilization of a labile glucocorticosteroid (such as budesonide as recited by instant claim 9) comprising the step of applying a moist heat to a suspension of a labile glucocorticosteroid for a sterilizing-effective time. And instant claim 2

is drawn to a method for the sterilization of a glucocorticosteroid (such as budesonide as recited by instant claim 9) comprising the step of heating (at a temperature of about 101°C to about 145 °C as recited by instant claim 4; by autoclaving, as recited by instant claim 5; and for about 2 to 180 minutes as recited by instant claim 6) an aqueous suspension of a glucocorticosteroid, wherein the glucocorticosteroid has a sufficiently low solubility in water and is used in a sufficient amount such that at least 50% (more specifically, at least 60% as recited by instant claim 3) of the glucocorticosteroid is in the form of a suspension during heating, the said suspension further comprising a surfactant as recited by instant claim 7.

7. *McAffer et al* teach a method for the sterilization of budesonide (i.e., a glucocorticosteriod, more specifically a labile glucocorticosteroid as recited by instant claims 1, 2 and 9) in a suspension further comprising polysorbate 80 (i.e., a surfactant as recited by instant claim 7) comprising autoclaving (as recited by instant claim 5) at 121°C (as recited by instant claim 4) for 15 minutes (as recited by instant claim 6) (Paragraph 0057). Furthermore, *McAffer et al* disclose that "the polysorbate surfactant was filter sterilized into a sterile vessel. To this vessel micronized budesonide was added aseptically... After addition the budesonide lay on top of the filtered polysorbate. Mixing was achieved by the use of a high shear mixing shaft. Twenty to twenty-five minutes of continuous mixing were required for the budesonide to go completely into suspension" (Paragraph 0038). As such, *McAffer et al* teach the method wherein the budesonide is used in a sufficient amount such that at least 50% (more specifically, at least 60% - as recited by instant claim 3) of the glucocorticosteroid is in the form of a suspension during heating. Accordingly, instant claims 1-7 and 9 are anticipated.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. **Claims 1-6 and 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Gentile et al* (US 2006/0140816 and EP 1454636).**

11. Instant claim 1 is drawn to a method for the sterilization of a labile glucocorticosteroid (budesonide or beclomethasone dipropionate as recited by instant claims 9-11) comprising the step of applying a moist heat to a suspension of a labile glucocorticosteroid for a sterilizing-effective time. And instant claim 2 is drawn to a method for the sterilization of a glucocorticosteroid (budesonide or beclomethasone dipropionate as recited by instant claims 9-11) comprising the step of heating (at a temperature of about 101°C to about 145°C as recited by instant claim 4; by autoclaving, as recited by instant claim 5; for about 2 to 180 minutes as recited by instant claim 6; and even more specifically at a temperature of about 121°C for about

20 to 30 minutes as recited by instant claim 10) an aqueous suspension of a glucocorticosteroid, wherein the glucocorticosteroid has a sufficiently low solubility in water and is used in a sufficient amount such that at least 50% (more specifically, at least 60% as recited by instant claim 3) of the glucocorticosteroid is in the form of a suspension during heating (even more specifically at a concentration of from about 15 mg/ml to about 150 mg/ml as recited by instant claims 12-13), the said suspension further comprising a surfactant as recited by instant claim 7 (at a concentration of from about 0.75 mg/ml to about 60 mg/ml as recited by instant claim 8).

12. *Gentile et al* (EP 1454636) teach a process for the sterilization of a glucocorticoid - which is synonymous with the term glucocorticosteroid as acknowledged by the instant Specification (Paragraph 0021) – and specifically, the glucocorticosteroid beclomethasone diproprionate – comprising the step of applying a moist heat to and heating (via autoclave) an aqueous suspension of a glucocorticosteriod and water (Paragraphs 0013-0014) wherein the "glucocorticoid:water ratio is preferably between 3:100 (about 30 mg/ml) to 10:100 (about 100 mg/ml)" (Paragraph 0016) and that "preferably steam sterilization was carried out at 121°C for 20 minutes" (Paragraph 0018). Accordingly, it is asserted that - absent evidence to the contrary - *Gentile et al* teach a process for the sterilization of a glucocorticoid wherein the glucocorticosteriod has a sufficiently low solubility in water and is in a sufficient amount such that at least 50% and more specifically at least 60% is in the form of a suspension during heating. As stated in *In re Best, Bolton, and Shaw*, "Where… the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product" 562 F2d 1252 (CCPA 1977).

See also *In re Fitzgerald* 619 F2d 67 (CCPA 1980): the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on." As such, *Gentile et al* teach the method recited by instant claims 1-6, 9 and 11-12. However, *Gentile et al* do not teach the method comprising ***budesonide*** as recited by instant claims 10 and 13, and as elected by Applicant. Nevertheless, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to substitute one known glucocorticosteroid (e.g., beclomethasone diproprionate) with another structurally and functionally similar glucocorticosteroid (butesonide) in the method taught by *Gentile et al* to sterilize said structurally and functionally similar glucocorticosteroid in the same way and with a reasonable expectation of success. Furthermore, the fact that similar methods taught by the prior art may have failed to effectively sterilize budesonide suspensions would not have reduced the skilled artisan's expectation of success since similar methods taught by the prior art also failed to effectively sterilize beclomethasone diproprionate. In particular, *O'Neill* discloses that moist heat sterilization of suspensions comprising glucocorticiods is not suitable for suspensions of fine particles intended for inhalation due to agglomeration and *Bernini et al* disclose that moist heat sterilization of suspensions comprising beclomethasone diproprionate resulted in significant increase in degradation products (Instant Specification, Pages 2-3). Yet, contrary to prior art, the method taught by *Gentile et al* did ***not*** provide significant crystal growth or result in degradation (Paragraphs 0052 and 0055) and did effectively sterilize the suspensions comprising beclomethasone diproprionate. Accordingly, the skilled artisan would have expected that the method taught by *Gentile et al* – which overcomes the problems taught by the prior art associated with sterilizing glucocorticosteroids (in particular beclomethasone diproprionate) using moist

heat – would successfully overcome the problems taught by the prior art associated with sterilizing structurally and functionally similar glucocorticosteroids such as budesonide.

13. Accordingly, for all of the foregoing reasons, instant claims 1-6 and 9-13 are rejected as *prima facie* obvious.

14. Instant claim 14 is drawn to the method of claim 13 further comprising the step of diluting the suspension to a pharmaceutically acceptable concentration. Gentile et al specifically disclose preparing final formulations that were mixed and diluted with water (Paragraphs 0071-0075 and Tables 10 and 11) which is asserted to encompass a pharmaceutically acceptable concentration as recited by instant claim 14.

15. **Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Gentile et al* (US 2006/0140816 and EP 1454636) as applied to claim 2 above, in further view of *Karlsson et al* (US 6,392,036)and *McAffer et al* (US 2003/0103864).**

16. Instant claims 7-8 are drawn to the method wherein the suspension further comprises a surfactant (claim 7), more specifically at a concentration of from about 0.75 mg/ml to about 60 mg/ml (claim 8). The inclusion of surfactants in glucocorticoid suspensions is well known in the art. Specifically, as discussed by *Karlsson et al*, "[t]o obtain an efficient dispersion of the glucocorticosteroid particles in the suspension, a surfactant may be used… The surfactants may also function as stabilizing agents" (Column 5, Lines 21-24). Indeed, *Gentile et al* disclose formulations further comprising a surfactant in the range recited by instant claim 8 (Paragraph 0067, Table 9 and Paragraph 0075, Table 10). Accordingly, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to include a surfactant as recited by instant claim 7, at a concentration within the range recited by instant

claim 8, to provide stabilizing agents and to obtain an efficient dispersion of budesonide particles in the suspension with a reasonable expectation of success. Although neither *Karlsson et al* nor *Gentile et al* disclose adding the surfactant to the suspension prior to sterilization by moist heat as recited by the instant method, it would have been within the purview of the ordinarily skilled artisan to include the surfactant ***before*** heat sterilization in view of *McAffer et al* which, as discussed above, disclose methods of sterilizing suspensions comprising budesonide and a surfactant via moist heating (Paragraph 0057). Although *McAffer et al* state that autoclaving the suspension comprising budesonide and a surfactant at 121°C for 15 minutes "resulted in unacceptable increases in the impurity levels present in budesonide suspensions [and thus is not] likely to be acceptable for the sterilization of budesonide" (Paragraph 0067), the skilled artisan would have not considered this a teaching away from the *prima facie* obvious method discussed above since, as previously noted, similar methods taught by the prior art also failed to effectively sterilize beclomethasone diproprionate. In particular, *O'Neill* discloses that moist heat sterilization of suspensions comprising glucocorticiods is not suitable for suspensions of fine particles intended for inhalation due to agglomeration and *Bernini et al* disclose that moist heat sterilization of suspensions comprising beclomethasone diproprionate resulted in significant increase in degradation products (Instant Specification, Pages 2-3). Yet, contrary to prior art, the method taught by *Gentile et al* (i.e., moist heat sterilization of suspensions comprising beclomethasone diproprionate at 121°C for 20 minutes) did not provide significant crystal growth or result in degradation (Paragraphs 0052 and 0055) and did effectively sterilize the suspensions comprising beclomethasone diproprionate. Accordingly, the skilled artisan would have expected that the method taught by *Gentile et al* – which overcomes the problems taught by

the prior art associated with sterilizing glucocorticosteroids (in particular beclomethasone diproprionate) using moist heat – would successfully overcome the problems taught by the prior art associated with sterilizing structurally and functionally similar glucocorticosteroids such as budesonide.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

18. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

19. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. **Claims 1-4, 6-7, 9-13 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6, 9-10, 13 and 15 of copending Application No. 11/667,872.**

21. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons: As discussed above, instant claim 1 is drawn to a method for the sterilization of a labile glucocorticosteroid (budesonide or beclomethasone dipropionate as recited by instant claims 9-11) comprising the step of applying a moist heat to a suspension of a labile glucocorticosteroid for a sterilizing-effective time. And instant claim 2 is drawn to a method for the sterilization of a glucocorticosteroid (budesonide or beclomethasone dipropionate as recited by instant claims 9-11) comprising the step of heating (at a temperature of about 101°C to about 145°C as recited by instant claim 4; by autoclaving, as recited by instant claim 5; for about 2 to 180 minutes as recited by instant claim 6; and even more specifically at a temperature of about 121°C for about 20 to 30 minutes as recited by instant claim 10) an aqueous suspension of a glucocorticosteroid, wherein the glucocorticosteroid has a sufficiently low solubility in water and is used in a sufficient amount such that at least 50% (more specifically, at least 60% as recited by instant claim 3) of the glucocorticosteroid is in the form of a suspension during heating (even more specifically at a concentration of from about 15 mg/ml to about 150 mg/ml as recited by instant claims 12-13), the said suspension further comprising a surfactant as recited by

instant claim 7 (at a concentration of from about 0.75 mg/ml to about 60 mg/ml as recited by instant claim 8).

22. The '872 application teaches a method for preparing a sterile suspension of a glucocorticoid comprising heating a glucocorticoid suspension (more specifically beclomethasone or budesonide as reicted by claims 9-10) at a concentration of from about 15 to about 300 mg/ml (claim 6) and wherein at least 60% is in suspension (claim 8) further comprising a surfactant (claim 3) at a temperature from about 122°C to about 138°C (claim 13) for at least about 30 minutes (claim 15).

23. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614